PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT EXAMINING OPERATION

Applicant(s): Susanne BRAKMANN et al.

Serial No: 10/089,841 Group Art Unit: 1797

Filed: September 30, 2002 Examiner: Lyle Alexander

Att. Docket No.: B1180/20005 Confirmation No.: 5272

For: STRUCTURED REACTION SUBSTRATE AND METHOD FOR PRODUCING THE SAME

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Susanne Brakmann, a citizen of Dortmund, Germany, hereby declare and state:

1. The resume attached as Exhibit A accurately reflects my professional credentials.

2. [DESCRIBE ANY POTENTIAL BIAS]I am a co-inventor of the subject matter described and claimed in the present application and a former employee of the assignee of the application.

3. I have reviewed the application and its prosecution history including the Final Rejection of February 15, 2008 and the Amendment of May 15, 2008.

4. I understand from my review of the Office Action that claims 17-21, 22-23 and 29-36 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent No. 4,299,920 to Peters in view of U.S. Patent No. 4,441,793 to Elkins and further in view of U.S. Patent No. 6,645,434 to Muramatsu et al., and that claims 27-28 stand rejected over those references in view of U.S. Patent No. 6,037,168 to Brown. I understand from attorneys for the assignee that 35 U.S.C. § 103(a) provides:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

5. While I am not an expert in patent law, my experience and educational background enable me to render an informed opinion as to the facts underlying the determination

of obviousness, including: (1) the scope and content of the prior art; (2) the differences between the claimed invention and the prior art; (3) the level of ordinary skill in the art; and (4) objective evidence of non-obviousness, such as commercial success, long-felt but unsolved need, failure of others, copying, and unexpected results. For the reasons discussed below, I believe that the facts support a conclusion that the claims are not obvious over the cited references.

6. Taken alone or in combination, Peters, Elkins, Muramatsu et al. and Brown fail to disclose or suggest the claimed reaction substrate comprising a flexible compartment layer of silicon rubber with a thickness from 0.5 mm to 4 mm perforated by an arrangement of holes, wherein the flexible compartment layer adheres to the surface of a glass plate substrate without adhesive such that the holes provide sample reservoirs with a sample volume from 1 nl to 10 µl, and variations of positions of the sample reservoirs in a direction perpendicular to a base plane are less than 250 µm over an entire surface of the base.

7. On the priority date of the present patent application (6 Oct 1999), it was well-known in the art that tools for high throughput screening (HTS) procedures, like reaction substrates, have to fulfill special requirements with regard to size, thickness and stability. A person having ordinary skill in the art at the time of the invention (a PHOSITA) would have possessed technical knowledge in the fields of microscopy and HTS procedures, and would have known that glass slides used in microscopy, such as those disclosed by Muramatsu et al., are very fragile objects. Even with the standard handling of such glass slides, like e.g., for mounting and viewing a specimen in a biological laboratory, there is always the risk of breaking the glass slide.

8. A PHOSITA would not have been motivated to consult, combine and modify the teachings of the cited references, which do not relate to HTS techniques and apparatus, with a reasonable expectation of successfully producing the claimed reaction substrate, which has claimed properties that make it suitable for use in HTS.

9. A PHOSITA would have lacked motivation to combine, with a reasonable expectation of success, a glass slide (or plate) having a thickness of about 150 nm with an adhering flexible compartment layer. The connection of the compartment layer with the glass plate is based on adhesion forces. A PHOSITA would have expected the glass plate to break under the influence of these adhesion forces during the placement of the compartment layer on

the glass plate and/or during the step of peeling off the compartment layer. Glass plates for microscopy were known to be fragile, as evidenced by the teachings of, e.g., U.S. Patent No. 4,427,634 at column 3, lines 37-38 ("The use of prior fragile, slippery glass slides is entirely eliminated."); U.S. Patent No. 5,292,000 at column 1, lines 19-22 ("These items are intended to protect the relatively fragile glass slide and to preserve the specimen smeared or deposited on the slide against contamination or physical damage."); U.S. Patent No. 6,014,210 at column 2, lines 20-22 ("However, slides are difficult to handle. They are difficult to pick up, hold and store. They are relatively fragile and may cause wounds in the form of cuts."); and U.S. Patent No. 6,908,678 at column 1, lines 15-17 ("It has been noted, however, that glass slide has several disadvantages as a substrate of biochips. Firstly, glass slide itself is fragile and has to be handled carefully."). The expectation of failure suggested by the known fragility of glass plates clearly would have outweighed any alleged motivation to examine slides with various types of microscopes (i.e., the motivation to combine alleged in the 27 Jun 07 Office Action at page 4).

10. The expectation of failure would have been even higher in view of the need to repeatedly adhere and remove the compartment layer through multiple iterations of an HTS procedure, particularly where the compartment layer is used in conjunction with a glass plate having a relatively large surface area to form microtiter or nanotiter plates adapted to receive numerous samples.

11. Given the anticipated fragility and flexibility of a glass plate having a thickness of about 150 nm, a PHOSITA would have not have expected a reaction substrate comprising such a glass plate as a base to exhibit sufficient stability such that variations of positions of the sample reservoirs in a direction perpendicular to a base plane are less than 250 μm over an entire surface of the base. This unexpected property of the claimed reaction substrates make them very well suited to use in HTS procedures in biotechnical and/or chemical research and development, as among other advantages, time-intensive readjusting, e.g. of microscope lenses, is not required in the z direction, perpendicular to the base.

I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine and/or imprisonment under Section 1001 of Title 18 of the United States

Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Date: June 12, 2008

S.B.

Name: Dr. Susanne Brakmann

Curriculum vitae

Personal data

Last name:	Brakmann
First name:	Susanne Marie
Date of birth:	February 24, 1964
Place of birth:	Osnabrück (Germany)
Citizenship:	German

Study

Oct. 1983–Nov. 1988	Study of Chemistry at the Technical University of Braunschweig
Nov. 1988	Diploma. Subject of thesis: "Synthesis of silicon–organic substrates for stereoselective biotransformations"
Dec. 1991	Ph. D. Examination. Subject of thesis: "Synthesis and stereoselective biotransformation of silicon– and germanium–organic compounds: Generation of optically active silanes and germanes using biocatalysis"
Feb. 2004	Post–doctoral lecture qualification (Habilitation) at the Technical University of Braunschweig (*venia legendi* for Bioorganic Chemistry)

Occupation

Apr. 1992–Dec. 1998	Scientific coworker of Prof. Dr. Manfred Eigen at the Max Planck Institute for Biophysical Chemistry, Göttingen (post–doctoral position)
May 1995–Dec. 1998	Group Leader. Subject: "Evolutionary Optimization of Enzyme Function"
Jan. 1999–Dec. 2000	Scientific employee, Evotec Biosystems AG, Hamburg, with place of work at the Max Planck Institute for Biophysical Chemistry, Göttingen
Jan. 2001–Jul. 2001	Scientific coworker of Prof. Dr. Manfred Eigen, Göttingen (group leader position)
Aug. 2001–June 2006	Head of the Junior Research Group "Applied Molecular Evolution" at the Biotechnological–Biomedical Center of the University of Leipzig
since July 2006	Lecturer and head of the research group "Directed Evolution", Department of Chemical Biology, Technical University of Dortmund